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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,257	01/09/2006	Gerd G. Kochendoerfer	AMLN-047	4540

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,257	KOCHENDOERFER ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *18-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-17 and the following species: Compound-polypeptide, specifically GRFN 1841 (composed of residues 131-174 of SEQ [D NO: 1); Chemical adduct-polypeptide, specifically GRFN 1846 (composed of residues 74-130 of SEQ, ID. NO: 1); Covalent bond in the linker-oxime; Reactive functional group: aminooxy; Water soluble protecting group: polyálkylene oxide, in the reply filed on 6/18/2007 is acknowledged.

Status of Claims

Claims 1-26 are pending

Claims 18-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions and species.

Claims 1-17 are under examination.

Specification

The abstract of the disclosure is objected to because the abstract is too long and not on a separate sheet. Correction is required. See MPEP § 608.01(b).

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicant's

cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Non-sequitur for "the same linkages" in claim 17.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-17 are rejected under 35 U.S.C. 102(a) as being anticipated by Kochendoerfer (WO 2002/200033) ('033 Patent)

The '033 World Patent discloses at page 10, lines 1-28:

A molecularly homogenous polymer-modified synthetic bioactive protein of the formula: Protein-Un-s1-B-s2-Polymer-s3-J* where Protein comprises a polypeptide chain of a ribosomally specified protein, where the polypeptide chain comprises one or more non-overlapping peptide segments covalently bonded by one or more chemical ligation sites, U is a residue of a unique functional group covalently bonded to a mutually reactive unique functional group of a side chain n of one or more amino acids of one or more of the non- overlapping peptide segments, where n is a discrete integer from 1 to 6, B is a 10 branching core having three or more arms that may be the same or different and may be present or absent, Polymer is a substantially non-antigenic water-soluble polymer that may be the same or different where B is present, J* is a residue of pendant group having a ***net charge under physiological conditions selected from the group consisting of negative, positive and neutral,*** and where s1, s2, and s3 are spacer or 15 ***linker moieties*** that may be the same or different, and may be individually present or absent. A preferred molecularly homogenous polymer-modified synthetic bioactive protein of the invention is one that is ***mono-disperse*** having a monomer molecular weight of greater than 25 kDa. In another embodiment, the invention is directed to a polymer-modified 20 synthetic bioactive protein having a polypeptide chain comprising an amino acid sequence of a ribosomally specified glycooprotein, ***where the polypeptide chain has one or more water-soluble polymers attached thereto.*** In a more preferred embodiment, one or more of the water-soluble polymers is covalently attached at one or more sites of the polypeptide chain that correspond to a glycosylation site of the 25 ribosomally specified glycoprotein. Preferred water-soluble polymers are **polyalkylene oxide**, polyamide alkylene oxide and derivatives thereof that are glyco-mimetic water-soluble polymers. The most preferred are polymer-modified synthetic proteins comprising a polypeptide chain of a cytokine glycoprotein.

The '033 World Patent further discloses at page 11, lines 4-20:

> The invention also is directed to ***methods of producing polymer-modified synthetic bioactive proteins of the invention.*** A preferred method for producing the synthetic bioactive proteins of the invention comprises chemically ligating peptide segments comprising non-overlapping amino acid sequences of a polypeptide chain of the polymer-modified synthetic protein, where one or more of the peptide segments used for ligation has a water-soluble polymer attached thereto at a user- defined and pre-selected site. The polymer-modified polypeptide chain may then be folded to produce a polymer-modified synthetic bioactive protein of the invention. Another preferred method for producing the synthetic bioactive proteins of the invention comprises chemically ligating peptide segments comprising non-overlapping amino acid sequences of a polypeptide chain of a synthetic bioactive polymer-modified protein of the invention, and attaching one or more water-soluble polymers to a side-chain of an amino acid at one or more chemical ligation sites thereof. The polymer-modified polypeptide chain may then be folded to produce a polymer-modified synthetic bioactive protein of the invention.

Further at paragraph bridging pp. 12 and 13:

> The invention particularly concerns such molecularly homogeneous water- soluble polymers wherein U is a residue of a functional group selected from the group consisting of acrylate, aldehyde, ketone, aminooxy, amine, carboxylic acid, ester, thioester, halogen, thiol, cyanoacetate, dipalmitoyl phosphatidylethanolamine, distearoyl phosphatidylethanolamine, epoxide, hydrazide, azide, isocyanate, maleimide, methacrylate, nitrophenyl carbonate, orthopyridyl disulfide, silane.

Claims 1-17 are rejected under 35 U.S.C. 102(a) as being anticipated by Kochendoerfer et al (WO 2002/19963)('963 World Patent.

The '963 World Patent discloses basically the same method as the above '033 World Patent. See e.g., page 13, line 11 up to

page 22, line 12. See the detail description of the method in the Examples starting at page 80, Example 1. Accordingly, the method of the '963 Patent fully meets the claimed method.

Claims 1-5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Coltart.

Coltart discloses at page 3475, paragraph 5.1.5 up to page 3488 a method of chemical ligation of peptides (step a, as claimed) with another peptides which would read on the broad claimed method of claim 1.

Claims 1-17 are rejected under 35 U.S.C. 102(b) as being anticipated Krepinsky (USP 5616698). (Based on the broad claim interpretation of any compound e.g., carbohydrate).

Krepinsky et al disclose at e.g., col. 2, line 35 up to col. 5 and the examples, e.g., Example 9.

> Polymer-supported liquid synthesis of peptides and oligonucleotides using polyethyleneglycol monomethylether (PEG) as support for the synthesis of oligomers of peptides and nucleotides has been described. Although in this reaction design the reactants are soluble in the reaction medium during the reaction itself, this methodology had not been considered for oligosaccharide syntheses.
>
> In our U.S. Pat. No. 5,278,303, we have shown that in the polyethylene glycol (polyethyleneglycol monomethylether [HOCH.sub.2 CH.sub.2 (OCH.sub.2 CH.sub.2).sub.n OCH.sub.3], where n is 80-160; PEG, average MW 5,000) supported synthesis of oligosaccharides, good anomeric specificity can be achieved by judicious application of chemical principles of oligosaccharide synthesis, without affecting other desirable facets of this synthetic design, i.e. the ease and speed with which the process is completed. In this approach a polymer-carbohydrate synthon is synthesized which is soluble under conditions of

glycosylation, and insoluble during the work-up of the reaction mixtures. This guaranteed solubility of the polymer-containing reactants during the reactions allows for reaction kinetics and anomericity control similar to that observed in solution chemistry. The oligosaccharide comprises at least two monosaccharide units by definition. At least one of the monosaccharides is suitably derivatized so as to allow attachment to the PEG or a derivative thereof. The oligosaccharide must be capable of being elaborated into a substance which is suitable for subsequent glycosylation. The glycosylation is performed under standard liquid-phase chemistry conditions which are well known in the art and are, of course, contingent upon the monosaccharide units and their associated linkages. Monitoring of the glycosylation reaction is easily achieved through nuclear magnetic resonance spectrometry. The number of additions of glycosylating agent needed for reaction completion may be more than one. The glycosylation agent may be any saccharide as long as it has an activated anomeric centre.

Claims 1-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Rose et al (6001364).

Rose discloses at e.g., the abstract:

Compositions of hetero-polyoximes of defined structure comprising a baseplate structure having a plurality of oxime bonds, wherein each oxime bond links a specifically active molecule to the baseplate. Also provided are novel baseplates having a plurality of oxime forming complementary reactive groups and novel specifically reactive molecules having an oxime forming complementary reactive group. Also provided by this invention are methods of preparing these novel compositions of matter by chemoselectively ligating via oxime bond formation a complementary orthogonal reactive group on the baseplate to a complementary reactive orthogonal group on a specifically active molecule. Methods of using these defined compositions of matter as well as pharmaceutical compositions comprising these defined compositions of matter and methods of their use are also provided by this invention. Provided by this invention are defined compositions of hetero-polyoximes of defined structure comprising a baseplate structure having a plurality of oxime bonds, wherein each oxime bond links a specifically active molecule to the baseplate. Also provided are novel baseplates having a plurality of oxime forming complementary reactive groups and novel specifically

reactive molecules having an oxime forming complementary reactive group. Also provided by this invention are methods of preparing these novel compositions of matter by chemoselectively ligating via oxime bond formation a complementary orthogonal reactive group on the baseplate to a complementary reactive orthogonal group on a specifically active molecule. Methods of using these defined compositions of matter as well as pharmaceutical compositions comprising these defined compositions of matter and methods of their use are also provided by this invention.

See further the Examples, which provide detail steps of the method of making the compounds. Accordingly, the specific process steps of Rose fully meets the broad claimed method.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0765. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw

August 20, 2007